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October 21, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: 2005D-0324 International Conference on Harmonization (ICH); Draft Guidance on M5 Data Elements and Standards for Drug Dictionaries; Availability

Merck & Co., Inc. (Merck) is a leading worldwide, human health products company. Through a combination of the best science and state-of-the-art medicine, Merck's Research and Development (R&D) pipeline has produced many important pharmaceutical products available today. These products have saved the lives of or improved the quality of life for millions of people globally.

Merck Research Laboratories (MRL), Merck's research division, is one of the leading biomedical research organizations. We have extensive experience in the development, licensure, and marketing of products and have used that experience to author the comments below. Our general comments on this draft guidance are followed by specific comments regarding sections of the draft guidance.

Merck commends the Food and Drug Administration (FDA) for publishing the ICH's draft guideline on data elements and standards for drug dictionaries, which are designed to assist in the development and maintenance of drug dictionaries. We agree that these standards should be harmonized and that this guideline appropriately outlines a sound concept to implement a process to standardize the Drug Dictionaries for approved medicinal products. We also agree that these standards, when finalized, will enhance the exchange of medicinal product information and ensure data consistency across the ICH Regions. With the development of unique identifiers (MedIDs; PhPIDs), controlled vocabulary (TermIDs), and data elements it seems that the process of harmonization can be achieved as medicinal products will hold a unique MedID, product name, and Marketing Authorization Holder, as well as TermIDs referring to specific active ingredients, pharmaceutical dose forms, routes of administration and units of measurements. While we believe the ideas and practices provided in the draft guidance are necessary to the success of this initiative, we believe the document could be enhanced by considering the following recommendations.

First, it is our understanding that the specific vocabularies, although not published in the *Federal Register* (FR), were published in the European Union (EU). Further, we believe the vocabularies will affect the implementation of the above referenced draft guidance.

Therefore, we request that FDA publish the vocabularies in the FR in order to provide an opportunity for the public to comment prior to final implementation.

We also request that FDA only require companies to submit the Term IDs for data elements taken from the controlled vocabularies. We presume that companies will be using the same Term IDs, and that regulatory health agencies can derive the text from the Term IDs. Therefore, it should not be necessary for companies to submit the term-text for these data elements.

Additionally, in our review of the document, we notice that the term "pharmaceutical" and terms associated with pharmaceuticals, such as "dose form", are used in many sections (e.g., section headings for 2.2.3, 2.3.7, 2.3.7.1 and 2.3.7.2, etc.). However, there are no examples for dosing terms provided for vaccines or biologics, nor are there specific subsections that address vaccine and biologics dosing terms.

Moreover, Section 2.3.6.3.4 Strength Unit Term, will be complicated for vaccine-manufacturers to implement since vaccine technologies are frequently changing, which can range from a rather simple titer for a live virus vaccine (measured in TCID50), to much more complex units. It would be almost impossible to create a static list given the rapid change in technologies with new products. This will somehow need to be accounted for when new products reach the market, such as the "free-form text" allowed under Section 2.3.6.3.6 Strength Description. Otherwise there will need to be a way for sponsors to get new measurement terms put into the dictionary in a timely manner prior to a vaccine's approval.

We believe the intent of the ICH is to include vaccines and biologics under the scope of this document and that the above sections are applicable to vaccines and biologics. Therefore, we request that FDA incorporate specific examples for vaccines and biologics throughout the guidance document.

In addition to the above general comments, we have provided the following comments that correspond to specific sections of the draft guidance.

Section 1.3 Scope of the Guideline
As stated above, we believe the intent of the ICH is to include pharmaceuticals, biologics, and vaccines under the scope of this guideline.
Recommendation: Therefore, we request that FDA include the following language in the final guidance:
"This guideline refers to approved pharmaceuticals, biologics, and vaccine products, and any combination of such medicinal products."

2.1.1 Medicinal Product Identifier – MedID
It is not clear from the draft guidance whether a product has one unique MedID worldwide, or if the same product has several MedIDs, one for each country where that

product is registered. The term "Worldwide unique MedID" could be interpreted that a product has one, not several, MedIDs.
Recommendation: We request that FDA clarify what is meant by "worldwide unique MedID", and provide examples of one product with several corresponding MedIDs from registration in different regions.

Further, this section of the draft guidance provides several examples. It is our understanding that a product can have several MedIDs for each package presentation. However, it is unclear from the examples provided how a MedID will look in a "real life" situation. Also, the exact format for the MedIDs is unclear from the examples provided, as different countries have different codes (e.g., the US example has 13 digits/letters, France has 9 digits/letters, etc.).
Recommendation: We request that FDA provide an enhanced, "real-life" example for the above section, i.e., include an example that provides a drug and its corresponding country, strength, and dosage combination (e.g., NEW DRUG in a 50 tablet bottle will be marketed in the US as a tablet = US XXXXXXX-X). This will provide companies with more concrete examples to determine how MedIDs will be incorporated for products. We also recommend FDA provide rationale for including different codes for different countries.

Additionally, the term "error detection code" is not defined.
Recommendation: We recommend that FDA include a definition of the term "error detection code" either in text of section 2.1.1 Methodolgy or in the Glossary section.

Lastly, it is unclear whether MedIDs will be used in adverse event reports (AE reports or AERs). Companies rarely receive full and complete Medicinal Product Names in these reports and in most cases would not be able to determine a specific MedID to report.
Recommendation: We request that FDA not utilize MedIDs in AE reports.

Section 2.1.2: PhPID
Recommendation: As stated above, it would be helpful to include enhanced examples in this section describing how these identifiers will be constructed for products registered to a specific country and its strength, strength unit, and dose form.

Additionally, the draft guidance states that the PhPIDs will be based on active ingredients.
Recommendation: We request that FDA include the word "active" before all of the examples. Additionally, we request that FDA provide examples explaining how a product with 2 or more active ingredients will be identified.

Section 2.3.5 Pharmaceutical Product Section
We believe the draft guidance is unclear with regard to whether the Agency will require regulated industry to provide Pharmaceutical Product data elements for all drug reporting activities (e.g., for other company's drugs listed in AE reports, prior/concomitant

activities (e.g., for other company's drugs listed in AE reports, prior/concomitant therapies in clinical trials, etc.). More specifically, the draft guidance is not clear as to whether FDA is requiring only the active ingredient elements or all drug elements.

Recommendation: If companies are required to provide the Pharmaceutical Product data elements for all drug reporting, we recommend that only the active ingredient be mandatory, and that the strength, dose, and route of administration data elements should be optional, as companies do not usually have this level of detail for other company's medicinal products.

In summary, we commend the Agency for its effort to incorporate the ICH's draft guideline designed to enhance the information exchange between regulators and industry. We appreciate the opportunity to work with the Agency on this initiative and we believe it can enhance the drug development process. We hope our recommendations help the Agency as it finalizes this important regulatory document.

Please feel free to contact me if you should encounter any questions regarding our comments.

Sincerely,

Brian Mayhew
U.S. Regulatory Policy